Polio eradication and after

C. R. Madeley

Burnfoot, Stocksfield, Northumberland, NE43 7TN, UK

It now seems highly likely that transmission of wild poliovirus will be interrupted throughout the world towards the end of 2002, and the disease of poliomyelitis will join smallpox as another that mankind has abolished by the use of a vaccine. At present, circulation in any community is confined to west and central Africa, particularly in Nigeria and the Horn of Africa, and to the Indian subcontinent. However, these areas also include countries of political instability and conflict, which have made surveillance and vaccine administration difficult.

Nevertheless, the interruption of the circulating wild virus will not totally remove the possibility of the disease recurring. Substantial numbers of poliovirus-containing specimens and other positive materials are still present in the deep freezes in laboratories of many kinds all over the world, and ensuring that these viruses do not escape will remain a challenge as long as any viable poliovirus remains.

Against this background, the World Health Organization Regional Office for Europe convened a Sub-Regional Meeting of National Co-ordinators for Laboratory Containment of Wild Polioviruses in Prague on 13–15 December 2000 to discuss the problems posed by these poliovirus-containing materials remaining within its region after 2002, and to hear how plans to evaluate and manage them in individual countries are progressing.

Anticipating the end of wild poliovirus circulation, the World Health Organization produced a 'WHO Global Action Plan for Laboratory Containment of Wild Polioviruses' [1] in 1999. This invited each country to establish a national inventory of poliovirus-containing materials, to encourage the destruction of stocks of such materials if they were no longer required and to arrange that those which are retained will be handled only at appropriate BioSafety (Handling) Levels (BSLs) in future. Representatives of 30 countries in Europe met with staff of WHO's European Regional Office from Copenhagen, Temporary Advisers and staff Members from the WHO Polio Eradication Programme Headquarters in Geneva for 2 days to exchange information on how far they had progressed towards implementing the recommendations made in the Plan.

Most countries had appointed a National Co-ordinator supported by a Containment Committee, and many had begun to send out questionnaires to laboratories to assemble an inventory of those with stocks of materials, either known to contain wild poliovirus or which might. This applies to material kept in freezers for more than 1 month, but not to that kept at room temperature in which the virus would not survive. There was also a practical need to get heads of laboratories to assess the contents of their freezers comprehensively rather than perfunctorily. This would mean that each laboratory Head would be required to take personal responsibility for the response by insisting on signatures, not just initials, at all levels of assessment, and signing the final version him/herself.

However, putting together a comprehensive list of all the relevant laboratories had proved, in many situations, to be more difficult than expected. Listing diagnostic virology laboratories was usually straightforward, but the list would also have to include other virology and microbiology laboratories in Universities and research Institutes, those under the aegis of a surprisingly long list of Government ministries, as well as a variable number of private laboratories and manufacturers of vaccines and disinfectants (who may test their products using stock wild polioviruses).

Immigrants and refugees, some of whom came from presently endemic areas (or who travelled to and from them), and who tended to slip outside regular medical services, also presented continuing problems over where specimens taken from them were examined and kept. Equally importantly, the list must include a wide variety of nonmicrobiologic laboratories, such as those studying aspects of nutrition both in their own countries and in, for example, developing countries. These laboratories may have made or retained survey collections of feces made in geographical areas where polio was endemic at the time, but without the present 'owners' necessarily being aware that these specimens will often contain infectious agents, including poliovirus. Hence, considerable lateral thinking would be needed to assemble an adequately comprehensive list of laboratories where viable poliovirus may remain as a potential hazard for the future.

When the list for each country is complete, a more detailed inventory of the actual contents of the freezers would have to be made. The collective expectation at the meeting was that this detailed scrutiny would turn up a considerable number of (often poorly labeled or anonymous) ampoules and bottles whose existence had long been forgotten, and many of those who had put them there would have moved, retired or even died. Taking such detritus out of deep-freezes would be valuable in itself. In this chase-the-virus exercise, the smaller European

Corresponding author and reprint requests: C. R. Madeley, Temporary Adviser, WHO, Burnfoot, Stocksfield, Northumberland, NE43 7TN, UK
Tel: +44 1661 842649
Fax: +44 1661 844514
E-mail: DickMadeley@aol.com

countries, with fewer laboratories to identify, have often made more progress with this inventory than the larger ones.

As soon as natural polio transmission has ceased, the requirements for adequate handling containment will rise. BSL 2/p(olio) should be the current norm for working with any kind of wild poliovirus and all potentially infectious material. From about 2003, the point defined as 1 year after the last wild strain has been isolated, BSL-3 biosafety standards must be applied to the handling of wild poliovirus and all potentially infectious material. After poliomyelitis is declared eradicated, projected to be in 2005, and as polio immunization is discontinued from, probably, 2010 (though it may be earlier in some countries), all work with wild poliovirus will have to be carried out at BSL 4, but such expensive and elaborate facilities will be available only in a very small number of places. At the same time, work with materials containing only live vaccine (OPV) strains will then have to be upgraded to BSL 3/p, because OPV escaping and passaging through a nonimmune population may revert to full virulence.

Poliovirus, whether as isolates, known positive specimens, neurologic or other pathologic specimens or as potentially infectious (but untested) feces, throat swabs or blood samples, will not escape from a freezer unaided. The virus-containing material will have to be taken out and used for some purpose involving amplification or giving it greater kinetic energy (e.g. by homogenization or being dropped) before it can reach and infect susceptibles. High titer virus (i.e. where the original amount of virus has been increased by culture, or by nucleic acid amplification techniques (such as reverse transcription PCR)), can present a hazard as it is, but unamplified samples pose a much smaller risk. Nonetheless, such materials will remain as potential time bombs if they are kept into an era in which there are (rapidly) declining levels of immunity in the population. One of the most efficient magnifiers of virus is a nonimmune individual of any age, and he/she will not necessarily show clinical signs or symptoms of disease despite being well able to disseminate high titer virus. If the need for containment is not taken seriously, it is not difficult to imagine a scenario in the future in which an unimmunized susceptible worker takes a stool specimen out of a freezer to assay fat levels, homogenizes it to make it uniform in consistency, infects himself and his colleagues and/or family, and accidentally initiates a new epidemic which would be very difficult to arrest. Other similar scenarios can be assembled without difficulty. The issue here is *not* the retention of specimens or virus, but ensuring that appropriate levels of validated Biosafety Handling are always used.

Aware of these possibilities, those at the meeting agreed that each national list of laboratories must be fully comprehensive and that there should be positive encouragement to discard any nonessential virus-containing materials, and to do so safely. What is classified as essential will have to be decided within each country, and WHO cannot compel the staff of any laboratory to dispose of material which has been collected or kept for good scientific reasons, and which they deem to be important. But it can insist that it is stored and handled only at the right BSL, and laboratories will find that setting up and using the necessary higher containment facilities *de novo* will incur significant and unavoidable costs. Moreover, few scientists would wish to court the widespread and intense international publicity that would focus on anyone who had the misfortune to reintroduce polio into the world, all the more so if it was shown to be due to sloppy technique or inadequate facilities. The combination of these two negative aspects may persuade some workers that retaining their stocks of material, of whatever kind, is simply not worth the risk.

Though widespread polio immunization will be discontinued around 2010, it is likely that pressure to maintain high levels of uptake will decline after 2005. Oral (live) polio vaccine (OPV) is associated with a low, but measurable, rate of complicating paralytic disease – a risk that can be justified in the face of circulating wild virus. As the latter disappears, both the risk and the cost of using OPV become increasingly unacceptable. Because the virus in the vaccine may revert to higher virulence after a single passage through man, some countries (of which Belgium is the latest) are already changing to inactivated polio vaccine (IPV) as an interim measure. IPV has for a long time been the vaccine of choice in the Netherlands and Scandinavia but it, too, is expensive and all countries will want to discontinue routine immunization with either vaccine as soon as there is agreement that it is safe to do so.

There is therefore powerful pressure to reduce the risk of wild virus escaping again, and the various national plans presented at the Prague meeting all had this as their ultimate aim. Once the laboratory inventories and catalogues are complete, and improved handling facilities are in place, preferably by March 2002 at the latest, each country will start to institute the required Biosafety Handling levels for these materials. Though some countries are further advanced than others at the moment, this should not be an unattainable goal. Further meetings are planned soon to include those countries not represented in Prague, and to continue to monitor progress throughout Europe.

Polio as a naturally occurring infectious agent is about to disappear. Making sure it never reappears will still require a great deal of work, and some clear thinking in justifying what should be retained in deep freezes in a wide variety of laboratories. It would be a monumental tragedy if so much hard work by so many people in every continent was ruined by a bit of carelessness or ignorance by one person. We (everyone involved) must work together to eliminate that possibility.

REFERENCE

1. World Health Organization. *WHO global action plan for laboratory containment of wild polioviruses.* Geneva: World Health Organization, 1999. (Copies may be requested from: WHO Vaccines and Biologicals, CH-1211 Geneva 27, Switzerland).